a central mail-pharmacy all linked via the INTERNET. The INVEST system uses Netscape Enterprise web server and the Oracle Relational Database to collect and store eligibility, treatment, follow-up and management data. A SUN Microsystems Ultrasparc running Solaris 2.5 provides web services and acts as a firewall equipped with 2 Ethernet adapters for a private network running on Windows NT. A RAID system assures no loss of service for drive failure. The entire system is backed up by FAX/phone. All study-related communications are in Swedish, and the system has high-level artificial intelligence to assure protocol correct data entry and permit physicians to customize drug combinations and dosing schedules, within the randomly-assigned treatment strategies. Pilot phase data on 150 patients from 15 sites will be presented. This approach we believe, is the forerunner of on-line clinical trials for the next century.

2:45

857-4 Rate and Extent of Left Ventricular Hypertrophy Regression: A Comparison of Angiotensin II Blockade With Irbesartan and Beta-Blockade

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Background: The effects of antihypertensive therapy with the AT_1 receptor antagonist irbesartan (IRBE) on the regression of left ventricular hypertrophy (LVH) were compared to those of atenolol (ATEN) in a double-blind, 48-week study.

Methods: 115 hypertensive men and women with left ventricular mass index (LVMI, by echocardiogram) >131 g/m^2 and >100 g/m^2, respectively, were randomized to receive IRBE 150 mg or ATEN 50 mg qd. For seated diastolic BP (SeDBP) >90 mm Hg, doses were doubled at 6 weeks, supplemental HCTZ or felodipine was added in 6-week intervals thereafter as needed. LVMI, SeBP, and neurohormones were measured at Weeks 12, 24, and 48.

Results: 48 IRBE and 53 ATEN patients completed the study. Baseline demographics were similar, mean BP, 162.4/103.6 mm Hg, LVMI (g/m^2) men, 151; women, 128. Mean ± SE changes from baseline were:

	IRBE		ATEN	
Wk	LVMI (95% CI)	SeDBP	LVMI (95% CI)	SeDBP
12	-5.76 ± 3.59 (-12.9, 1.5)	-9.2 ± 1.5	-0.45 ± 2.95 (-6.4, 5.5)	-12.0 ± 1.0
24	-9.12 ± 3.72 (-16.6, -1.6)	-12.2 ± 1.2	-4.51 ± 2.94 (-10.4, 1.4)	-14.3 ± 1.1
48	-19.66 ± 4.07 (-27.9, -11.5)	-18.0 ± 1.4	-11.97 ± 2.93 (-17.9, -6.1)	-16.6 ± 1.1

By 48 weeks, 34% of IRBE and 45% of ATEN patients remained on monotherapy. Renin decreased with ATEN; renin and AII increased with IRBE consistent with AT_1 blockade. 67% of ATEN and 34% of IRBE patients reported adverse drug experiences.

Conclusions: Despite similar BP reductions with both regimens, LVH regressed sooner and to a greater degree with IRBE compared with ATEN. IRBE produced superior tolerability and end organ protection. The results support a role for AII in the development of LVH.

3:00

857-5 Effects of Single Drug Antihypertensive Therapy on Left Atrial Enlargement in Hypertension

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Background: Left atrial (LA) enlargement (E) is common in hypertension. We previously reported ↓ in av LA size on echo at 1 yr only with hydrochlorothiazide (HCTZ) despite efficacy of HCTZ, captopril (CAPT) and atenolol (ATEN) for BP and LV mass reduction. However the influence of LAE as well as age, race, and body weight (covariates known to influence LA size) on efficacy of drugs for reduction of LA size is unknown.

Methods: We used 2D-targeted M-mode echo to measure LA size in 587 men (av BP 152 ± 14/99 ± 3 mmHg, av age 59 ± 10 yrs, 40% LAE) in a 15 center randomized double-blind trial of six active drugs; HCTZ, CAPT, ATEN, clonidine (CLON), diltiazem (DILT) and prazosin (PRAZ). Drug effects were statistically adjusted for age, race, body weight, and baseline LA size.

Results: While no changes occurred at 8 wks, at 1 yr pts with LAE had ↓ in LA size [all p < 0.05, adjusted means (mm) ± S.D.] with HCTZ (-4.2 ± 1.1), ATEN (-4.2 ± 1.1), CAPT (-3.2 ± 1.1), CLON (-2.9 ± 1.0) and DILT (-2.9 ± 1.1) but not PRAZ (-0.3 ± 1.1, pNS). Pts with normal baseline LA size had a ↓ in LA size (p < 0.05) with CAPT (+2.7 ± 1.0) and CLON (+3.8 ± 1.0), with a trend for ↓ with HCTZ (-1.6 ± 1.0; 95% CL -3.5–+0.3).

Conclusion: ↓ in LA size with antihypertension therapy requires prolonged treatment. The magnitude of ↓ differs between classes of agents and is affected by prior LAE, but not by interdrug differences in BP control or in reduction of LV mass.

3:15

857-6 Diuretics Preserve the Circadian Blood Pressure Profile in Hypertensive Patients

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Background: Normally blood pressure (BP) decreases during the night in normotensives and most hypertensives. The loss of nocturnal BP fall is known to be associated with an impaired prognosis. Little is know about the relative ability of different antihypertensive classes in preserving the diurnal pattern of BP. Thus we evaluated the circadian BP profile in a large cohort of hypertensive patients.

Methods: We enrolled 1502 consecutive subjects (aged 17–88 years, 50.8% males), who had been referred for assessment of hypertension. All patients performed a 24-hour ambulatory BP monitoring. A subset with stable therapy was identified (n = 704) and divided into five groups according to the drug treatment regime: ACE-inhibitors, β-blockers, calcium channel blockers, diuretics, or combined antihypertensive agents.

Results: Patients on diuretics had significantly lower systolic BP during night-time compared to patients treated with ACE-inhibitors (p < 0.003), β-blockers (p < 0.02), and antihypertensive drug combination (p < 0.0001), but not versus calcium channel blockers (p = 0.1). Patients on diuretics presented a greater nocturnal diastolic BP fall compared to patients treated with ACE- inhibitors (p < 0.003), or antihypertensive drug combination (p < 0.02), but not versus patients with β-blockers (p = 0.1) or calcium channel blockers (p = 0.1).

Conclusion: Preservation of nocturnal BP fall using diuretics may contribute to the known reduction of cardiovascular morbidity and mortality in this class of drug. Utilization of diuretics as first-line antihypertensive therapy could result in a better cost-benefit ratio.

858 Metabolic Stress on Infection and Vascular Function

Tuesday, March 31, 1998, 2:00 p.m.–3:30 p.m.
Georgia World Congress Center, Room 257W

2:00

858-1 Infection With Chlamydia Pneumoniae Accelerates the Development of Atherosclerosis and Treatment With Azithromycin Prevents it in a Rabbit Model

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Chlamydia pneumoniae infection is associated with atherosclerosis by serologic studies and detection of bacterial antigen within plaque. We sought to evaluate a possible etiologic role in an animal model.

Thirty New Zealand white rabbits were given 3 separate intranasal inoculations of either *C. pneumoniae* (N = 20) or saline (N = 10) at 3 week intervals and fed chow enriched with a small (0.25%) amount of cholesterol. Infected and control rabbits were then randomized and begun on a 7 week course of azithromycin or no therapy. After three months, the rabbits were euthanized and sections of thoracic aortas blindly evaluated microscopically for maximal intimal thickness (MIT), percentage of luminal circumference involved (PLCI), and plaque area index (PAI) of atherosclerosis. MIT was increased in infected rabbits compared with uninfected controls: 0.55 (SE 0.14) mm vs 0.16 (SE 0.06) mm, p = 0.022, whereas MIT for infected rabbits receiving antibiotics was similar to uninfected controls (0.20 [SE 0.03]) and less than that of infected, untreated rabbits (p = 0.021). PLCI and PAI also increased after untreated but not treated infection. Immunofluorescent chlamydial antigen was detected in 2/9 untreated, 3/10 treated, and 0/10 control animals.

Conclusion: Intranasal *C. pneumoniae* infection accelerates intimal thickening in rabbits given a modestly cholesterol-enhanced diet and treatment with azithromycin after infectious exposure prevents it. These findings strengthen the etiologic link between *C. pneumoniae* and atherosclerosis and should stimulate further studies.